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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/447,681	11/23/1999	JACK A. ROTH	INRP.003--2/	4103

7590 09/27/2002

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	19

DATE MAILED: 09/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/447,681	ROTH, JACK A.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication app ars on th cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67 and 86-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67 and 86-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The request filed on May 13, 2002 in paper no. 18 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/447,681 is acceptable and a CPA has been established. An action on the CPA follows.

Applicant's arguments filed May 13, 2001 in paper no. 18 have been fully considered but they are not persuasive. The amendment has been entered. Claims 66 and 86-89 are pending.

The rejection of claim 67 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention has been overcome.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 67 remains provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22,29 and 32-34 of copending Application No. 09/668,532 for reasons of record as set forth in the office action mailed April 18, 2001, paper no. 12.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The rejection is maintained for reasons of record as set forth in the office action mailed April 18, 2001, paper no. 12. Applicant has not submitted arguments as to why the rejection is improper, but has

indicated a willingness to filed a terminal disclaimer if appropriate. It is noted by the examiner that this application has now been allowed. However, the examiner does not have access to the allowed claims. It would be appreciated if, in response to this office action, applicant would supply a copy of the allowed claims.

Claims 67 and 86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 8-10, 12, and 15-18 of U.S. Patent No. 6,410,010. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 67 and 86-89 comprises all the elements that are recited in claims 2, 3, 8-10, 16 and 18 of '010.

Present claim 67 is to an adenovirus vector comprising a wild type 53 gene under the control of a CMV promoter. Present claim 86 is to an adenovirus vector comprising a wild type p53 under the control of a promoter. Claims 1-3 and 8-10 of '010 are to a recombinant adenovirus which carries an adenovirus vector construct comprising an expression region encoding p53 under the control of a CMV immediate early promoter, claim 5 of '010 is to an adenovirus vector construct comprising an expression region encoding p53 under the control of a CMV immediate early promoter, claim 12 of '010 is to a recombinant adenovirus which carries an adenovirus vector construct comprising an expression region encoding p53 under the control of a promoter, claims 15-18 of '010 are to a recombinant adenovirus which carries and adenovirus vector construct comprising an expression region encoding

p53 under the control of a CMV immediate early promoter and claim 17 of '010. It is noted that each of the claims in '010 cited in this rejection contain language to the level or effect of p53 expression. However, this language does not offer a structural alteration to the claims and thus is not given weight in this rejection. The adenovirus vectors of claims 67 and 86 would express inherently to the same level.

Claims 67 and 86 of the present application and claims 1-3, 5, 8-10, 12, and 15-18 each require the same elements or obvious variations of elements. Present claims 67 and 86 state adenovirus vector. This is inherently the recombinant adenovirus of claims 1-3, 8-10, 12, 15, and 17. Further, given the adenovirus vector of present claims 67 and 86, the adenovirus vector construct of claims 5, 16 and 18 of '010 would be obvious as present claim 67 would contain such a construct. Present claims 67 and 86 state wild-type p53, whereas each of claims 1-3, 5, 8-10, 12 and 15-18 of '010 state p53. However, the specification of '010 defines p53 as including wild type p53. Present claims 67 and 86 state CMV promoter, whereas each of claims 1-3, 5, 8-10, and 15-18 state CMV IE promoter. However, the CMV IE promoter is a type of CMV promoter, and thus present claims 67 and 86 are generic to claims 1-2, 8-10 and 15-18 of '010. Claim 12 of '010 states promoter, and thus the CMV promoter of present claims 67 and 86 is an obvious promoter given the '010 definition of promoter. Thus at the time of the present invention, it would have been obvious to the ordinary artisan modify the recombinant adenovirus or adenovirus constructs of claims 1-3, 5, 8-10, 12 and 15-18 to make the adenovirus vectors of present claims 67 and 86.

Claims 86-89 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 12 of U.S. Patent No. 6,410,010. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference

claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 86-89 comprise all the elements that are recited in claim 12 of '010.

Claims 86-89 are to adenovirus vectors comprising a wild type p53 gene under the control of a promoter, and where the promoter is the β-actin promoter, the SV40 promoter or the RSV promoter. Claim 12 of '010 is to a recombinant adenovirus that carries an adenovirus vector construct comprising an expression region encoding p53 under the control of a promoter. The adenovirus vectors of present claims 86-89 inherently contain an adenovirus vector construct. The specification of '010 defines p53 as including wild type 53, and the specification defines promoter as being an actin promoter, an SV40 promoter or an RSV promoter. Thus the elements of present claims 86-89 are found in claim 12 of '010.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 67 remains, and newly added claims 86-89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record as set forth in the office action mailed April 18, 2001, paper no. 12, and as now applied to claims 86-89, repeated below, and the rebuttal arguments in the office action mailed February 12, 2002.

The instant specification does not contemplate adenoviral vectors comprising a wild type p53 gene operably linked to a promoter, the specific embodiments where the promoter is a CMV, RSV, β-actin or SV40 promoter. The examiner has read and re-read the specification in its entirety and has not been able to determine such support that would satisfy the written description portion of 35 USC §112. At page 7, lines 1-7, discusses the evidence in the art that mutations of the p53 gene cause lung cancer; page 9, line 6-8, states that the vector construct for introducing a wild type p53 gene under the control of a -actin promoter is a retroviral vector; page 9, lines 14-15, states wild type p53 constructs; page 14, lines 26-27 and 31-34, discusses antisense RNA expressed from any promoter; page 15, lines 1-5, state that the -actin, RSV, SV40 and a CMV promoters are used to express antisense RNA; page 25, lines 4-5, discuses that mutations of a p53 gene are the most frequently found mutations in human cancers; page 26, lines 13-16, states that the inventors feel that the reversal of a single altered genetic event in a cancer cells can potential reverse critical features of the malignant phenotype; page 27, lines 24-28, states that the protocol focuses on the regional delivery of wild type p53 for the treatment of tumors; page 33, lines 9-11, states that adenovirus can be used to introduce an antisense intron; and page 66, lines 10-18, states that tumors should be resected and that to the residual tumor the appropriate retroviral vector is to be injected. Further, the examiner has found at page 63, lines 30-34, it is stated that antisense p53 in a retrovirus is used; page 64, lines 27-31, states a retroviral construct comprising p53 cDNA; page 65, lines 7-22, states retrovirus mediated transfer of p53 cDNA and pages 67, line 15 to page 68, line 1, states risks of retroviruses. At no place in the specification is the invention of the claims clearly set forth so that the reader would realize that which applicant perceived as their invention at the time of filing. In the places where adenovirus or the specific classes of promoters claimed are disclosed, each such disclosure is within the context of antisense RNA production. Therefore the specification lacks a written description of the invention as claimed.

MPEP 2163.02 states:

> Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., Vas-Cath, Inc. v.

> Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Electronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").
> The subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement. If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

It is maintained that the present specification provides no such reasonable clarity to those skilled in the art that applicant was in possession of the claimed invention.

Applicant provides seven "bullets" that they feel support the enablement of the present claims. The examiner has read these seven bullets and does not agree with applicant's reasoning and evidences. The discussion of the seven bullets, referred to as 1-7, in respective order, will provide the examiner's reading of these citations from the specification.

1. At page 9, lines 6-12, the specification states generally "in one specific embodiment, the invention concerns vector constructs for introducing wild type p53 genes ..."; "... wherein the wt-p3 is placed under the control of the β-actin promoter, and the unit is positioned in reverse orientation into a retroviral vector." There is no mention of adenovirus vectors at this citation. Therefore this citation does not support written description of the claimed invention.

2. At page 61, lines 29-30, the only vector discussed to express wild type p53 in both orientations is a retroviral vector. As there is no mention of adenovirus vectors, this citation fails to provide the needed support for written description.

3. At page 8, line 25 or page 9, line 4, the effect which is stated to be achievable with other promoter/vector constructs, is the enhanced expression when the promoter in the retrovirus is reversed with regard to other promoters within the retrovirus (page 8, lines 25-31). A complete reading of the paragraph bridging pages 8-9 indicates the "phenomenon" is this effect. The generic disclosure to "other promoter/vector constructs" in no fashion leads the artisan to adenovirus vectors containing any promoter, or the CMV, β-actin, SV40 or RSV promoters as claimed in any particular orientation.

4. At page 14, lines 21-23, are not seen as supporting written description. A reading of the specification from at least page 5, line 7 to at least page 16, line 10, shows that this citation is embedded in a discussion of antisense technology. The only contemplation provided at this cite is the use of adenovirus to express antisense RNA to inhibit tumor growth.

5 and 6. At page 15, lines 1-4, and page 14, line 35 or page 15, line 2, each citation is embedded in a paragraph that begins "the particular promoter that is employed to control the expression of the antisense RNA ....". A reading of the paragraph in its entirety results in the conclusion that the β-actin promoter is not the only promoter that can be used to express antisense RNA, but the RSV, SV40 and CMV promoters also are contemplated to express antisense RNA. There is no contemplation of the claimed invention. Thus, this citation fails to provide support.

7. At page 16, lines 5-10, the specification states "while the retrovirus construct aspect .... concerns the use of a β-actin promoter in reverse orientation, there is no limitation on the nature of the selected gene ..."; "thus, the invention concerns the use of antisense coding constructs as well as "sense" constructs that encode a desired proteins. The contemplation is clearly for other genes expressed in the sense or antisense orientation from the β-actin promoter in a retroviral vector. There is no contemplation of any expression from an adenovirus vector, sense or antisense, at this citation.

Thus, a complete reading of the specification, and a reading of applicant's citations in context, fails to provide written description for the claimed invention.

Applicant has provided a declaration by Dr. Philip Hands (App. B) to provide evidence that one of ordinary skill in the art would find applicant in possession of the claimed invention at the time of filing. Declarant Hinds states that he bases his conclusion on page 9, lines 6-8 and page 14, lines 21-23.

With regard to the citation at page 9, lines 6-8, the specification states generally "in one specific embodiment, the invention concerns vector constructs for introducing wild type p53 genes ..." This is a generic statement without any mention of adenovirus. With regard to the citation at page 14, lines 21-23, a reading of the specification from at least page 5, line 7 to at least page 16, line 10, shows that this citation is embedded in a discussion of antisense technology. The only contemplation provided at this citation is the use of adenovirus to express antisense RNA to inhibit tumor growth. There is no disclosure in either citation that supports adenovirus comprising wild type p53 gene operably linked to a CMV promoter or any promoter.

Applicant states that the examiner has not provided evidence to rebut applicant's arguments of written description. The examiner has provided in each office action where this rejection has been made an analysis of the specification, and an analysis of the specification with regard to applicant's or delcarants citations. This is more than argument. This constitutes arguments accompanied by factual evidence. Applicant's citation of MPEP 2163.04 is proper for written description, but the relevant portion states:

> The examiner has the initial burden of **presenting by a preponderance** of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. (Emphasis added)

The examiner in providing a detailed analysis of the specification, including applicant's a arguments and declarant's citations, provides a preponderance of evidence and provides for the examiner's burden.

Applicant is denied benefit of the early priority dates claimed, as they do not provide a written description of the claimed invention. To be granted priority under 35 USC § 120,

the claims must comply with 35 USC § 112, first paragraph. The specifications of 07/960,513, filed October 13, 1992 and 07/665,538, filed March 6, 1991 do not provide written description for claimed adenoviral vectors.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 67 and 86 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Liu et al (1994) Cancer Res. 54, pages 3662-3667.

Lui teaches an adenovirus vector comprising a wild-type p53 gene operably linked to an CMV promoter (page 3662, col. 2, parag. 4). Thus, Lui clearly anticipates the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 86-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (1990) Science 250, 1576-1579 and Stratford-Perricaudet et al (1990) Human Gene Therapy 1, 241-256 in view of Wilkinson et al (1992) Nucleic Acids Res. 20, 2233-2239, Colicos et al (1991) Carcinogenesis 12, 249-255, Rajan et al (1991) J. Virol. 65, 6553-6561 and Hitt et al (1990) Virol. 179, 667-678.

Claims 86-89 are drawn to adenovirus vectors comprising a wild type p53 gene or a human wild type p53 gene under the control of a promoter, where the promoter can be a CMV promoter, a β-actin promoter, an SV40 promoter or an RSV promoter.

Chen et al teach retroviral vectors comprising a wild type human p53 operably linked to the retroviral LTR (page 1576, col. 3, Figure 1). Chen et al teach that wild type 53 is expressed in transduced Saos cells, and that the transduced cells failed to form colonies on soft agar or tumors in nude mice (page 1577, col. 2, line 12 to col. 3, line 8). Chen et al also teach that wild type p53 counters the transformation phenotype conferred by a mutant p53 when both genes are present in equal gene dosage (page 1579, col. 1, parag. 1 to col. 2, line 1 and col. 2, parag. 1, lines 25-28). Stratford-Perricaudet et al teach the correction of an enzyme deficiency related disorder in mice (abstract). The mice are mutant for ornithine transcarbamylase and when treated with an adenovirus vector comprising an ornithine transcarbamylse DNA sequence operably linked to the adenovirus major late promoter, the mice exhibit a reversal of the mutant phenotype (page 251, parag. 1, lines 1-3). Chen et al and Stratford Perricaudet et al do not teach adenoviral vectors comprised of a wild type p53 gene under the control of a CMV promoter, a β-actin promoter, an SV40 promoter or an RSV promoter. Wilkinson et al teach the production of an adenovirus expression system where a CMV promoter regulates expression of lacZ (page 2234, col. 1, parag. 5, lines 1-3). Wilkinson et al also teach that the adenovirus-CMV system can be used to studies of gene expression and gene regulation (page 2238, col. 2, parag. 4, lines 1-4). Colicos et al teach an adenovirus vector comprising a T4 *denV* gene operably linked to the RSV promoter, the RSV LTR (page 250, col. 1, parags. 4-7, figure 1 and figure 2). The vector, Ad5denV, was shown to partially complement the excision repair deficiency in primary fibroblasts from xeroderma pigmentosa patients (page 254, col. 1, parag. 2, and page 253, figures 6 and 7, and Table 1). Rajan et al teach an adenoviral vector comprising a cDNA sequence encoding an SV 40 small-t antigen operably linked to an SV40 promoter (page 6554, col. 1, parag. 2). Rajan et al teach that the expression of the SV40 small-t antigen results in the transactivation of adenovirus EII early promoter (page 6557, col. 1, line 13 to col. 2, line 4). Hitt et al teach an adenovirus where the expression of the E1A gene is regulated by a human β-actin promoter (page 670, col. 1, line 12 to col. 2, line 2, and figure 1). Hitt et al teach that E1A production is 3 to 5 times higher than by wild type adenovirus (page 675, col. 2, parag. 1, lines 11-16).

Thus it would have been obvious to the ordinary artisan at the time of the instant invention to determine the reversal of a transformed phenotype by expressing in an adenoviral vector comprising a human wild type p53 gene operably linked to a promoter, and specifically where the promoter is a CMV promoter, a β-actin promoter, an SV40 promoter or an RSV promoter, given the teachings of Chen et al that wild type p53 can reverse the transformed phenotype of tumor cells when the cells are transduced with a retroviral vector comprising a human wild type p53 gene operably linked to a promoter and the teachings of Stratford-Perricaudet et al that adenoviruses are useful for human gene therapy protocols in view of the teachings of Wilkinson et al, Colicos, Rajan et al or Hitt et al that a CMV promoter, a β-actin promoter, an SV40 promoter or an RSV promoter functions within a adenovirus to regulate expression of a sequence encoding a protein of interest. All that is required that there is a reasonable expectation of success and motivation to make the claimed adenovirus vectors. Motivation is provided by Chen et al in stating that expression of p53 in cells Saos cells which lack functional p53 reverts the transformed phenotype, and that such suggests possible clinical use of p53 gene replacement (page 1579, col. 1, parag. 1, line 1 to col. 2, line 1 and col. 2, lines 21-25). Additional motivation comes from Stratford-Perricaudet et al offer that states that adenoviral vectors can be used in human gene therapy procedures to restore impaired metabolism (abstract, last line). Promoter testing was known within the art at the time of filing to determine those promoters that provided the best expression.

Applicant argues that the combination of references in the previous office action do not provide the requisite motivation. Applicant asks why would the ordinary artisan be motivated to modify the teachings of Chen.

In response, the examiner has provided an new reference that teaches the use of adenoviral vectors in gene therapy protocols. Very often researchers test and try different vector/promoter constructs in vitro, such as the Saos cell system of Chen et al, to determine which construct would provide better expression of the desired product. As Chen et al taught that p53 expressed from a retroviral vector reversed the transformed phenotype in Saos cells, the ordinary artisan at the time of filing, given the teachings of Stratford-Perricaudet would have been motivated to use an adenoviral-p53

construct in Saos cells to determine if that construct would have greater efficiency and perhaps greater applicability to a gene therapy setting. In keeping with an attempt to obtain the best expression of p53, the ordinary artisan at the time of filing would have been motivated to substitute an RSV, SV40 or β-actin promoter, given the teachings that these promoters were active in cells, to perfect their p53 expression protocol.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
August 9, 2002